

THE EMBRYOLOGY OF THE ARTERIES OF THE BRAIN

Arris and Gale Lecture delivered at the Royal College of Surgeons of England

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by

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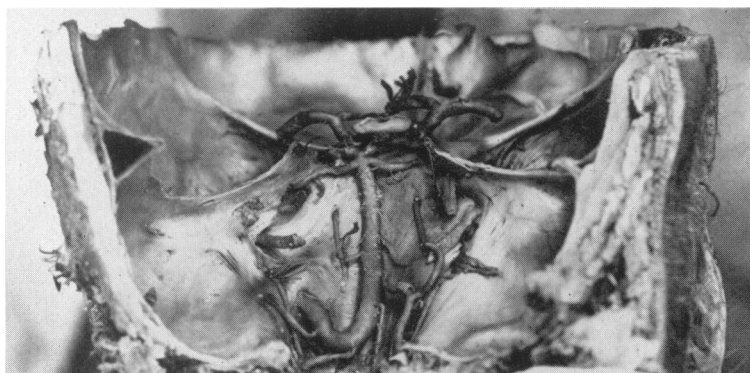
A LITTLE OVER 300 years ago, Edward Arris donated to the Company of Barbers and Surgeons a sum of money "upon condicion that a humane Body be once in every yeare hereafter publicquely dissected and six lectures thereupon read in this Hall if it may be had with conveniency, and the Charges to be borne by this Company". Some years later, Dr. Gale left an annuity to the Company for a similar purpose and it is interesting to note that the first Gale lecturer was a Dr. Havers, whose name is still associated with the Haversian canals in bone. The study of anatomy has changed in many ways since those days and it must be a long time since an Arris and Gale lecturer actually took his text from the cadaver. However, in deference to the wishes of our benefactors, I should like at least to commence this lecture by showing you part of a dissection (Fig. 1) which a colleague, Dr. E. D. Morris, and I prepared some years ago for use in an oral examination. We found that in this subject the left internal carotid artery in the neck gave off a large branch which passed upwards and backwards to enter the skull through the hypoglossal canal. In the posterior cranial fossa this artery looped caudally and then passed forwards in the midline to form the basilar artery which was joined by a pair of very small vertebral arteries. While trying to find an embryological explanation for the course of this remarkable vessel we were surprised to find how few accounts of the development of the arteries of the brain have been published in the past. The most recent and most comprehensive description is to be found in the beautifully illustrated paper by Padget (1948), but even this classical account cannot be said to cover all the stages of development. This is partly due to the fact that the usual method of study of the vascular system in human embryos is that of serial sectioning followed by reconstruction. This is a most time-consuming process so that it is impossible to study a large number of embryos, which is, of course, desirable if development is to be followed in detail. Furthermore certain vessels, notably the posterior cerebral artery, do not develop fully until the embryo is too large to allow serial sectioning and, finally, it is difficult accurately to reconstruct a dense vascular plexus.

In an attempt to overcome these difficulties it was decided to study the development of the arteries of the brain in injected rat embryos. With a few exceptions which I shall mention later, the developing vascular system in the rat bears a very close resemblance to that of the human embryo and it was considered that a number of gaps in our knowledge might thus be

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filled. The technique of the preparation, injection and dissection of the embryos has already been given in detail (Moffat, 1957, 1959) and need not be repeated here. Approximately 250 rat embryos have been studied, and, in addition, 11 human foetuses were injected with Neoprene latex and dissected.

A very early stage in the development of the arteries of the brain may be seen in Figure 2, which shows the right side of a 3.7 mm. embryo. The second and third aortic arches are present and the continuation headwards of the dorsal aorta forms the primitive internal carotid artery. Upon reaching the forebrain it gives a large branch, the primitive maxillary artery, which passes ventral to the optic stalk and forms the main blood supply to the cranial pole of the brain. The internal carotid then divides into its cranial and caudal rami. The former is very small at this stage,



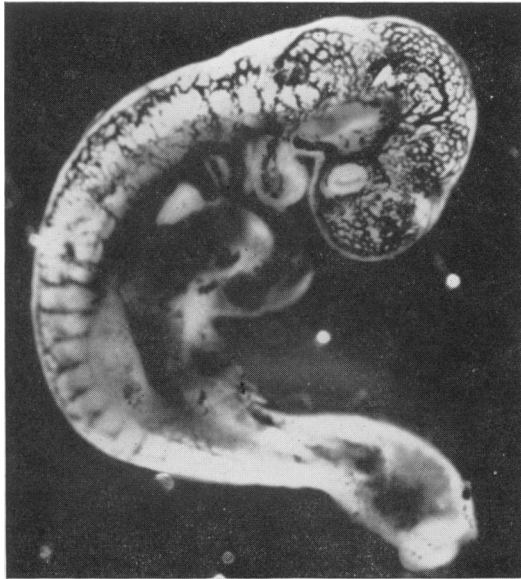
From Fig. 5, E. D. Morris, D. B. Moffat, Anat. Rec., 125: 701.

Fig. 1. The posterior cranial fossa of a case in which the basilar artery was a branch of the internal carotid artery and entered the skull through the hypoglossal canal.

and after passing dorsal to the optic stalk it almost immediately breaks up into a capillary plexus. The caudal ramus, however, is large and passes back to reach the midbrain flexure, giving a number of branches to the brainstem as it does so. In the plexus on the side of the midbrain the mesencephalic artery, with its characteristic caudal sweep, is just beginning to appear. The dorsal intersegmental arteries may be seen arising from the dorsal aorta caudal to the aortic arch region. The second intersegmental artery is damaged, but the first, the pro-atlantal artery of Padget (1954), is just beginning to show its headward prolongation—the lateral longitudinal artery—which runs cranially on the side of the hindbrain.

New vessels now rapidly differentiate out of the capillary plexus which covers the brain and these may be seen in Figure 3. The internal carotid still gives a large primitive maxillary branch and it then divides into well marked cranial and caudal rami. The cranial ramus passes forwards,

dorsal to the optic stalk, and its first branch is the anterior choroid artery which disappears from view behind the rapidly expanding telencephalic vesicle. It next supplies several branches to the telencephalon, one of which will later enlarge to form the middle cerebral artery, and then gives a recurrent branch which passes ventrally and caudally to join up with the primitive maxillary artery so that the optic stalk is now completely surrounded by a peri-optic arterial ring. The continuation of the cranial ramus is known as the primitive olfactory artery since it is mainly concerned in the supply of the developing nasal region. The caudal ramus of the internal carotid follows the concavity of the midbrain flexure and at the



From Fig. 2, D. B. Moffat, Am. J. Anat., 108: 17-30.

Fig. 2. Right side of a 3.7 mm. embryo.

summit of the curve it gives off in turn the diencephalic and the mesencephalic arteries which usually have a common trunk of origin but which arise separately in this specimen. The caudal ramus ends by uniting with its fellow of the opposite side to form a midline vessel which almost immediately divides again to form the right and left anterior cerebellar arteries. These correspond to the superior cerebellar arteries in man. In the hindbrain region the lateral longitudinal artery is now large and the pro-atlantal artery, just after its origin from the aorta, communicates with a longitudinal neural plexus which lies on either side of the midline along the ventral surface of the hindbrain. This plexus, from which the basilar artery will later develop, gives a large branch to supply a plexus on the thin roof of the hindbrain. This is the posterior cerebellar artery,

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corresponding to the anterior inferior cerebellar artery of human anatomy. Its origin from the plexus is concealed by the internal carotid artery in Figure 3 and for the same reason a series of important tributaries of the plexus are not visible. They may be seen, however, in Figure 4, which shows the ventral aspect of the hindbrain of a 5.2 mm. embryo. A segment of each of the internal carotid arteries has been left attached to the specimen although the carotid on the left of the photograph is difficult to see against the black background. It may now be seen that each longitudinal neural plexus is fed mainly by several large presegmental branches

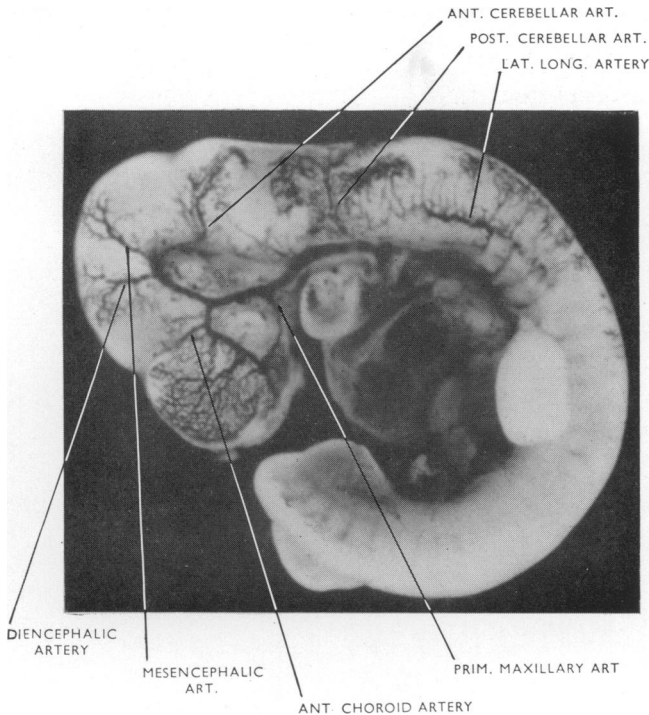
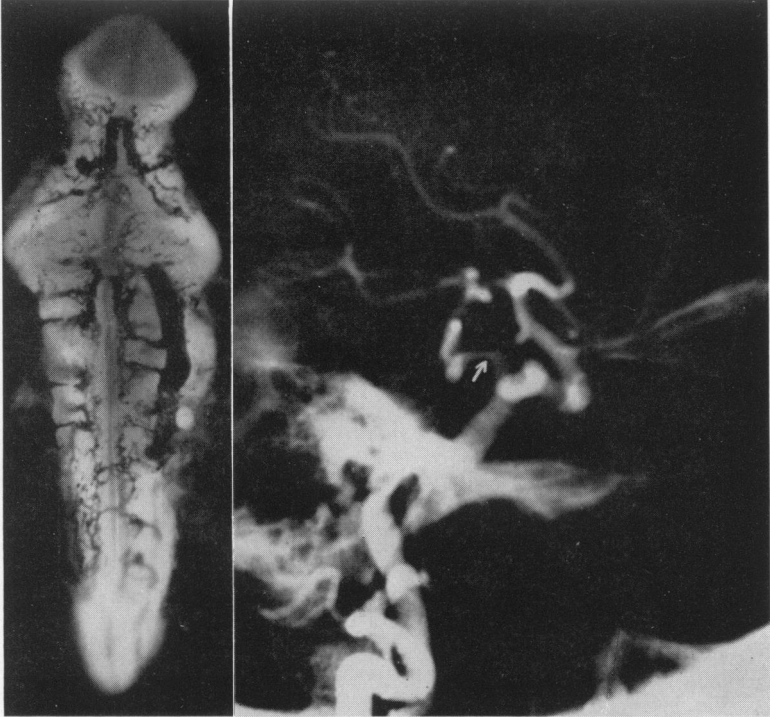


Fig. 3. Left side of a 5.3 mm. embryo. Note the peri-optic ring.

of the internal carotid arteries although it does communicate cranially with the caudal ramus of the carotid and caudally with the pro-atlantal artery. The plexuses are still in an early stage of development, but already a few transverse vessels link them across the central non-vascular strip. The presegmental arteries vary to some extent in their number and position, but two of them are constant—one near the trigeminal ganglion and another in the vicinity of the otocyst. These two vessels, the primitive trigeminal and otic arteries, have been described or depicted by a number of authors in human embryos and Padget (1948) has given a very complete description. One or more presegmental arteries are also found in relation

to the hypoglossal rootlets and these, too, have been described in human embryos by several authors, the most complete account being that of Schmeidel (1932), who found from one to three hypoglossal arteries in each of four human embryos between 5 and 8 mm. in length. The presegmental arteries are of some importance, firstly because they provide the main blood supply to the hindbrain for a considerable period and, secondly, because they occasionally persist into adult life and may be of some



By courtesy of Dr. A. S. Bligh.

Fig. 4 (*left*). Ventral view of the hindbrain of a 5.2 mm. embryo to show the presegmental arteries. A segment of each of the internal carotid arteries has been left attached to the specimen.

Fig. 5 (*right*). A case of persistence of the primitive trigeminal artery (arrowed).

clinical importance. By far the commonest vessel to persist is the primitive trigeminal artery, which forms a wide communication between the intracranial portion of the internal carotid artery and the basilar artery (Fig. 5). I have only been able to find one case of persistence of the otic artery in the literature (Altmann, 1947) and a persistent hypoglossal artery, too, is a rarity, only four cases having been described. One of these, of course, is the case shown in Figure 1, although it is believed that a

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further portion of the embryonic vascular network in addition to the hypoglossal artery had persisted in this case (Morris and Moffat, 1956).

The next stage of development is seen in Figure 6, which shows a 7.6 mm. embryo. The presegmental arteries have now disappeared, but otherwise all the arteries of the previous stage are still present. The diencephalic and mesencephalic arteries have a common stem of origin from the caudal ramus of the internal carotid and this stem also gives off a third branch. This is the posterior choroid artery which passes cranially on the side of the brainstem and disappears behind the telencephalic vesicle. In the hind-brain the basilar artery is beginning to develop from the longitudinal

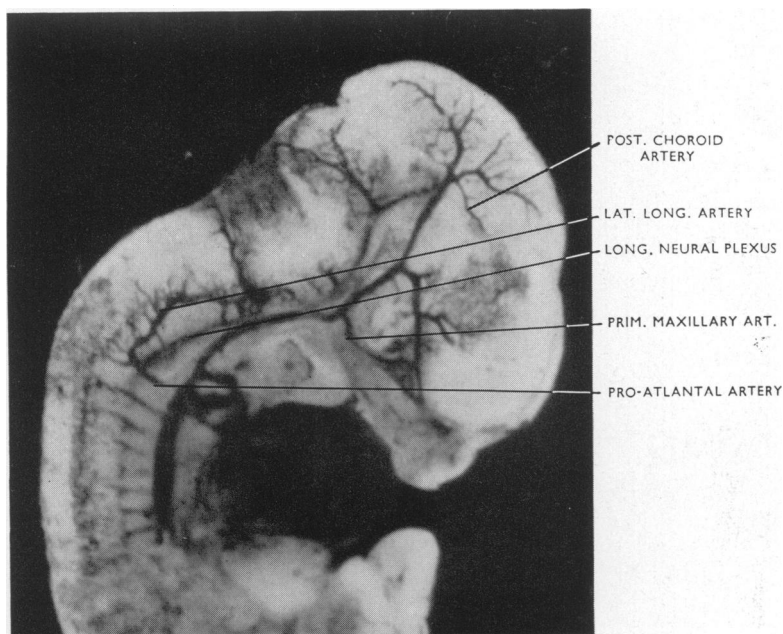


Fig. 6. Right side of a 7.6 mm. embryo. For description see text.

neural plexuses. It is fed by the pro-atlantal artery via the caudal unfused portion of the longitudinal neural plexus which is now connected to the prominent lateral longitudinal artery by one or two transverse vessels.

It will now be most convenient to consider the development of certain of the main arteries of the brain independently, commencing with the anterior cerebral artery. Figure 7 shows the ventral aspect of the fore-brain of a 7.2 mm. embryo. The large primitive olfactory arteries have been divided in order to remove the brain. The ventral portion of the peri-optic ring formed by the primitive maxillary artery and the recurrent branch of the primitive olfactory is well shown, and from the recurrent

branch a number of vessels stream towards the longitudinal fissure of the brain. These later become reduced in number until only one on each side remains. At the same time the primitive maxillary artery regresses and the distal part of the recurrent branch dwindles in size until it is represented only by a small vessel which supplies the region of the future optic chiasma (Fig. 8). Thus the proximal part of the anterior cerebral artery is formed from the primitive olfactory artery, its recurrent branch and one of the cranially directed branches of the latter. The remainder of the recurrent

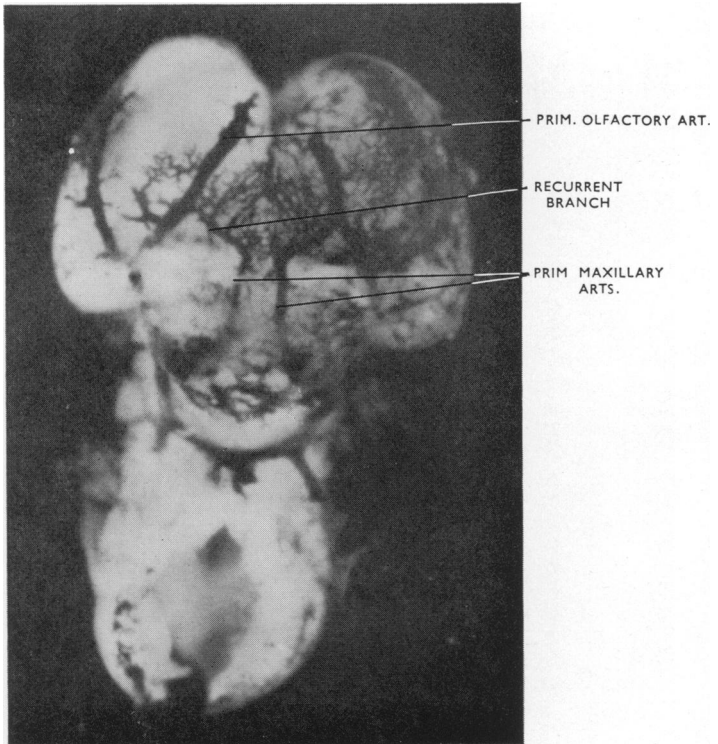


Fig. 7. Ventral aspect of the forebrain in a 7.2 mm. embryo.

branch becomes a chiasmal branch of the anterior cerebral artery. The portion of the anterior cerebral artery which lies between the two cerebral hemispheres differentiates *in situ* from the general capillary plexus. In this region the two arteries, in the rat, unite for a part of their course to form a single midline vessel, a condition which is sometimes found in man (Mitterwallner, 1955; Alpers *et al.*, 1959), and the two vessels then separate again to supply the medial aspect of the cerebral hemisphere. Each artery in addition gives a choroid branch to the anterior part of the choro-

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dal fissure. This branch, in the rat, persists into adult life, as does the primitive olfactory artery.

There are a number of interesting points of comparison between the appearance of these vessels in the rat and in the human embryos described by Padget (1948). The primitive olfactory artery has a similar history in both species up to the 18 mm. stage of human embryos. By this time it has diminished in size in the human and in Padget's 24 mm. embryo it is

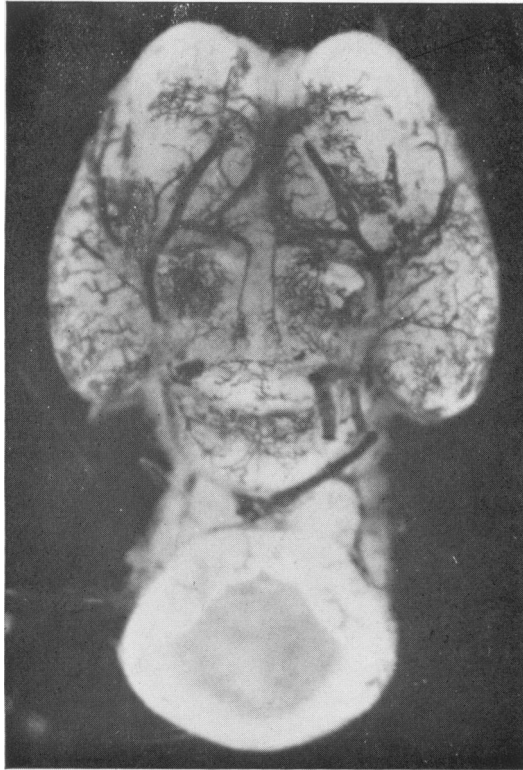


Fig. 8. Ventral aspect of the forebrain in an embryo of approximately 11 mm. to show a later stage in the development of the anterior cerebral artery.

very small although it still supplies the nose. Its stem will eventually form a small inconstant striate branch of the anterior cerebral artery. Ecker (1951) and Berk (1961) have both described cases of persistence of the primitive olfactory artery, but these authors were apparently referring to this striate branch. I have recently seen a case of persistence of the main part of the primitive olfactory artery in a 71-year-old male who died of carcinoma of the stomach. The left anterior cerebral artery gave off a

branch which passed forwards to pierce the dura of the anterior cranial fossa. After supplying a few small dural branches it divided into three vessels which passed through the cribriform plate and supplied the nasal cavity.

It seems likely that a peri-optic ring is present in man as well as in the rat, although no authors have specifically mentioned it. The primitive maxillary artery is certainly a prominent vessel in the human embryo and in Padget's Figure 3, which shows a 5.5 mm. embryo, this vessel is large and, together with what appears to be a recurrent branch of the primitive olfactory artery, almost completes the ring. The stem of a possible recurrent branch is also seen in several other reconstructions in Padget's



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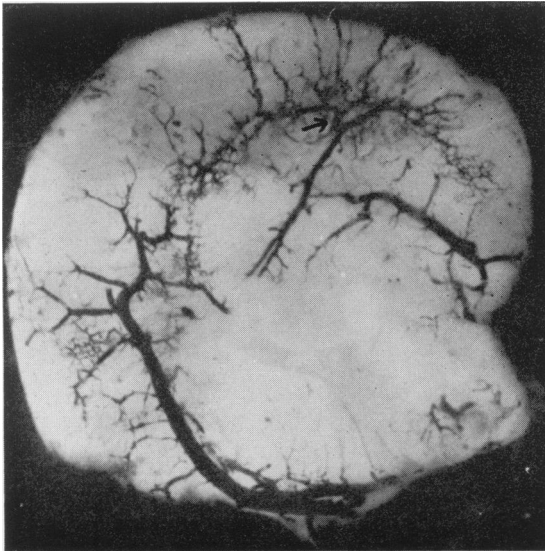
Fig. 9. The medial aspect of the right telencephalic vesicle of an 11.7 mm. embryo.

paper. Elze (1907), too, illustrates an almost complete peri-optic ring in a 7 mm. human embryo. As has been stated, the distal portion of the recurrent branch of the primitive olfactory artery in the rat forms a chiasmal branch of the anterior cerebral artery and it is significant that similar branches are found in man (Steele and Blunt, 1956; Dawson, 1958). An interesting anomaly was found in five of the rat embryos studied. In these specimens the cranial ramus of the internal carotid terminated as the middle cerebral artery, the primitive olfactory being a continuation of the primitive maxillary artery, i.e. the ventral part of the peri-optic ring had persisted instead of the dorsal segment. This seems to be the explanation of the case described by Robinson (1959) in an adult male in which the anterior cerebral artery passed inferior to the optic nerve. This explana-

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tion probably also applies to two cases described by Bassett (1949), who found aneurysm formation of an anomalous vessel which arose from the internal carotid artery and passed below the optic nerve.

The choroid branch of the anterior cerebral artery of the rat persists into adult life. A similar choroid branch is present in the human embryo (Bremer, 1943; Padget, 1948), but Padget found it only up to the 39 mm. stage and states that it does not persist. It was present, however, in most of the human foetuses in the present series, even in the largest—a foetus of 187 mm. in which it was represented by a fairly large artery which reached the tela choroidea by curving around the splenium of the corpus callosum.



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Fig. 10. Medial aspect of the right telencephalic vesicle of a 14.0 mm. embryo. The posterior choroid artery has been detached from the brainstem and remains adherent to the specimen. Its lateral branch is shown by the arrow.

Lazorthes *et al.* (1956) have found a similar artery to be occasionally present in the adult.

The next vessel which deserves close attention is the posterior cerebral artery. The vessels which contribute to its formation are the anterior and posterior choroid, the diencephalic and the mesencephalic arteries and these have already been seen in Figure 6. In this embryo, however, it is not possible to see the termination of either of the choroid arteries because they disappear behind the overhanging telencephalic vesicle. In Figure 9 one vesicle has been removed from the diencephalon and is viewed from the medial side. It can now be seen that the anterior choroid artery, as well as supplying the choroidal fissure, sends a large branch to the posterior

part of the telencephalon, where it breaks up into a capillary plexus which already shows some signs of a longitudinal orientation. There are often two or more of these telencephalic branches and the distal part of the posterior cerebral artery will develop from the plexus which they supply. These are transitory vessels and the blood supply of the posterior pole of the cerebrum is soon taken over by a laterally directed branch of the posterior choroid artery. The main trunk of this vessel is closely adherent to the diencephalon and ends in the choroidal fissure, and its lateral branch has to bridge the gap between the diencephalon and the telencephalic vesicle in order to supply the latter. As soon as the lateral branch is fully formed, the telencephalic branch or branches of the anterior choroid artery disappear so that the lateral branch becomes directly continuous with the longitudinal vessel which, by now, has begun to form in the capillary plexus on the medial wall of the telencephalic vesicle (Fig. 10) and which will later form the distal part of the posterior cerebral artery. The diencephalic artery at this stage sends branches to the side of the brainstem, a lateral (telencephalic) branch which reinforces the cranial end of the posterior cerebral artery and a terminal branch which enters the choroidal fissure. The completed posterior cerebral artery is made up of a part of the caudal ramus of the internal carotid, the common trunk of the posterior choroid, diencephalic and mesencephalic arteries, the stem of the posterior choroid artery, its lateral branch and the longitudinal vessel which developed in the capillary plexus of the telencephalic vesicle. That part of the posterior choroid artery which lies distal to its lateral branch becomes relatively smaller and forms a choroid branch of the posterior cerebral artery, while the diencephalic artery similarly forms a choroid branch which itself sends a branch to the medial side of the telencephalon. The mesencephalic artery forms the stem of the midbrain branches of the posterior cerebral artery.

The development of the posterior cerebral artery in the human has not previously been studied although Mall (1904), Bremer (1943) and Padget (1948) have commented on the possible fate of some of the embryonic vessels involved and Padget (1956) has stated that the diencephalic artery is represented by at least one adult posterior choroid artery. In a previous paper (Moffat, 1961) I suggested, on the scanty evidence then available, that the development of the human posterior cerebral artery is probably similar to that of the rat, and the examination of a larger number of human specimens since then has supported this statement although it has become apparent that the medial and lateral choroid branches as previously described in the rat do not correspond exactly with similarly named branches in the human. The human medial posterior choroid artery (Galloway and Greitz, 1960) is developed from the distal portion of the embryonic posterior choroid artery, while the lateral posterior choroid artery, or arteries, are derived from the diencephalic artery. Furthermore, considerable variation was seen in the human specimens and although the

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study of a much larger series is obviously desirable and is, in fact, proceeding, it seems likely that in some embryos the distal part of the posterior cerebral artery is derived from the lateral (telencephalic) branch of the diencephalic artery rather than from the lateral branch of the posterior choroid artery.

Turning now to the hindbrain, we have seen in Figure 6 that the lateral longitudinal artery becomes connected to the caudal part of the longitudinal neural plexus by one or two transverse branches which pass between the rootlets of the hypoglossal nerve. The later development of this

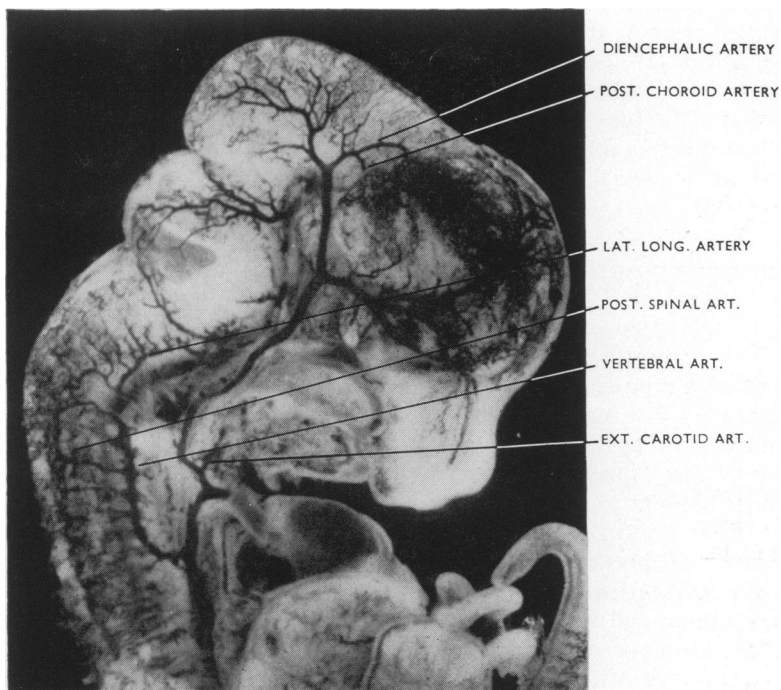


Fig. 11. Right side of 9.7 mm. embryo. Note the relation of the lateral longitudinal artery to the hypoglossal nerve rootlets.

region may be seen in Figure 11. The cervical part of the vertebral artery has now appeared as a longitudinal anastomosis between the upper seven intersegmental arteries; another more dorsally situated longitudinal chain of vessels will later form the posterior spinal artery. The lateral longitudinal artery has now lost its origin from the pro-atlantal artery and is supplied from the longitudinal neural plexus as a result of the enlargement of one of the transverse vessels mentioned above. The pro-atlantal artery has a dorsal branch which forms the stem of origin of the posterior spinal artery and which also anastomoses with dorsal branches of the lateral

longitudinal artery. Thus both posterior spinal and lateral longitudinal arteries become branches of the intracranial part of the vertebral artery, although the former may arise directly from the latter as a result of enlargement of the anastomosis of their dorsal branches. The lateral longitudinal artery is a prominent feature at certain stages of human development although many authors do not mention it. Padget (1948) called it the "primitive lateral basilo-vertebral anastomosis", but the present name is preferred as this vessel is more than a secondary anastomosis between the branches of the longitudinal neural plexus and is, in fact, as Schmeidel (1932) recognized, a primary and important branch of the pro-atlantal artery. A study of the reconstructions of this region by Schmeidel (1932) and Padget (1948) suggests that the developmental history of the arteries of this region in the human bears a close resemblance to that of the rat except for the fact that in the human embryo much of the lateral longitudinal artery disappears and one of its dorsal branches persists to form the posterior inferior cerebellar artery.

I should like to close by discussing an unsolved but fascinating problem, namely that of the pathogenesis of intracranial "berry" aneurysms. Among the possible causes or contributory factors which have been blamed at one time or another are hypertension, arterial disease, medial defects and a dilatation of remnants of thin-walled embryonic vessels. I should like to suggest a possible *locus minoris resistentiae* at which aneurysm formation may occur as a result of hypertension or arterial disease. As can easily be seen in most of the specimens illustrated here, the main embryonic arteries develop as channels running through a capillary network. Occasionally a small part of this network may persist along the course of an artery in the embryo and this results in the artery being duplicated for a short part of its course. This phenomenon is illustrated in Figure 12 (inset) where it will be seen that the appearance is such that it could be described as a localized dilatation of the vessel with a central perforation, and it is noteworthy that a collateral branch is always given off from one or other of the two channels. As might be expected, this appearance is often seen in early embryos, but with decreasing frequency in the later stages of development and it is of interest to speculate whether such formations persist into adult life. They have, in fact, been found in many of the arteries of adult brains (Moffat, 1960; Hassler, 1961) and in the anterior communicating artery by Busse (1921) and Emrich (1923). They take the form of a "pillar" stretching across the lumen of a slightly dilated portion of the artery at a bifurcation or at the origin of a collateral branch (Fig. 12). The "pillars" do not necessarily have a central perforation—they may consist of a solid mass of smooth muscle and connective tissue or they may have a central core of adventitia.

There are two reasons why these formations might provide a *locus minoris resistentiae*. Firstly, the divergent streams of blood caused by the pillar projecting into the lumen will cause an increased lateral pressure on

the arterial wall. The second, and possibly more important reason, concerns the law of Laplace which has been applied to blood vessels by Burton (1954). In general terms this states that the greater the radius of the vessel, the greater the tension required in the wall to prevent distension of the vessel. Thus if the arterial walls become weakened or the blood pressure increases, a local dilatation of a vessel will provide a relatively weak region which is liable to become distended and in this way a vicious circle is set up since the increased radius further increases the ease of distension. I have been unable to find any remnants of a "pillar" in the few aneurysms which I have so far examined, but Busse (1921) and Emrich (1923) have described cords of smooth muscle and connective tissue running across the



Fig. 12. A segment of a human middle cerebral artery which has been opened to show a "pillar" at the origin of a collateral branch. The inset shows part of the injected anterior cerebral artery of a rat foetus in which a portion of the foetal capillary network has persisted to form a perforated dilatation of the vessel.

lumen of a number of aneurysms and one such specimen is illustrated in Busse's Abb. 5.

It seems that some of the early Arris and Gale lecturers carried out their tasks with commendable thoroughness, for in 1739 it was ordered that "the demonstrator shall not for the future continue his lecture longer than three days after the public lecture is over; and on no account longer than six o'clock at night on those days". I think, therefore, that I should now conclude this account of the embryology of the arteries of the brain and it only remains to express to the Council of the Royal College of Surgeons my appreciation of the honour and privilege of being appointed to an Arris and Gale Lectureship.

ACKNOWLEDGMENTS

It is a pleasure to express my thanks to the numerous colleagues who have made available to me the foetal material, and to Mr. A. Welch and

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APPOINTMENT OF FELLOWS AND MEMBERS TO CONSULTANT POSTS

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